

APPENDIX B
MARKED-UP VERSION OF REPLACEMENT PARAGRAPHS

Page 1, before "Background of the Invention", insert the following paragraph:

Related Application Information

This application is a divisional of application serial no. 09/610417 filed July 5, 2000, which is a divisional of application no. 09/299,549, filed April 26, 1999, which is a divisional of application no. 09/031,392, filed February 26, 1998.

Paragraph that bridges page 1, line 25 to page 2 line 29:

The invention described herein relates to the discovery and characterization of a cDNA encoding GLUTX, a human glucose transporter protein. The nucleotide sequence of a cDNA encoding GLUTX is shown in [Fig. 1] Figs. 1A-1E. The deduced amino acid sequence of GLUTX is shown in [Fig. 2] Figs. 2A-2D. GLUTX is predicted to include 12 transmembrane domains. The first transmembrane domain extends from about amino acid 52 (intracellular end) to about amino acid 71 (extracellular end). The second transmembrane domain extends from about amino acid 108 (extracellular end) to about amino acid 128 (intracellular end). The third transmembrane domain extends from about amino acid 141 (intracellular end) to about amino acid 159 (extracellular end). The fourth transmembrane domain extends from about amino acid 166 (extracellular end) to about amino acid 189 (intracellular end). The fifth transmembrane domain extends from about amino acid 204 (intracellular end) to about amino acid 221 (extracellular end). The sixth transmembrane domain extends from about amino acid 233 (extracellular end) to about amino acid 252 (intracellular end). The seventh transmembrane domain extends from about amino acid 317 (intracellular end) to about amino acid 338 (extracellular end). The eighth transmembrane domain extends from about amino acid 355 (extracellular end) to about amino acid 375 (intracellular end). The ninth transmembrane domain extends from about amino acid 383 (intracellular end) to about amino acid 404 (extracellular end). The tenth transmembrane domain extends from about amino acid 413

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(extracellular end) to about amino acid 437 (intracellular end). The eleventh transmembrane domain extends from about amino acid 449 (intracellular end) to about amino acid 472 (extracellular end). The twelfth transmembrane domain extends from about amino acid 481 (extracellular end) to about amino acid 499 (intracellular end). GLUTX nucleic acids and polypeptides, as well as molecules which increase or decrease expression or activity of GLUTX, are useful in the diagnosis and treatment of disorders associated with aberrant hexose transport.

GLUTX protein has some sequence similarity to a number of known glucose transporters [(Fig. 3)] (Figs. 3A-3D).

Paragraphs 2-4 on page 10 at about lines 12-19:

[Fig. 1 is a depiction] Figs. 1A-1E depict the nucleotide sequence (SEQ ID NO:1) of human GLUTX.

[Fig. 2 is a depiction of] Figs. 2A-2D depict the predicted amino acid sequence (SEQ ID NO:2) of human GLUTX.

[Fig. 3 is] Figs. 3A-3D depict a comparison of the amino acid sequences of GLUTX (SEQ ID NO:2), GLUT1 (SEQ ID NO:3), GLUT2 (SEQ ID NO:4), GLUT3 (SEQ ID NO:5), GLUT4 (SEQ ID NO:6), and GLUT5 (SEQ ID NO:7).

Paragraph that bridges page 11 at about line 29 to page 12 at about line 13:

The GLUTX gene was identified as follows. A variety of public and proprietary sequence databases were searched using an approach designed to identify putative glucose transporters. This search led to the identification of an EST which was thought likely to encode a portion of a gene having some similarity to genes encoding previously identified glucose transporters. Two PCR primers (TGTTTCCTAGTCTTTGCTACA; SEQ ID NO:8 and TTGTAAAGGCCTTCCATT; SEQ ID NO:9) based on the sequence of the identified EST were used to screen a human mixed tissue cDNA library. This screening resulted in the identification of a probe which was used to screen the human mixed tissue cDNA library. This screening led to the identification of a number of

putative glucose transporter clones. A number of these clones were sequenced and ordered to arrive at a complete sequence for GLUTX. The nucleotide sequence of GLUTX is shown in [Fig. 1] Figs. 1A-1E. The predicted amino acid sequence of GLUTX is shown in [Fig. 2] Figs. 2A-2D.

First paragraph on page 28 at about lines 2-15:

To design functionally equivalent polypeptides, it is useful to distinguish between conserved positions and variable positions. This can be done by aligning the amino acid sequences of GLUTX that are obtained from various organisms or by aligning GLUTX with other identified glucose transporters, *e.g.*, GLUT1 (SEQ ID NO:3), GLUT2 (SEQ ID NO:4), GLUT3 (SEQ ID NO:5), GLUT4 (SEQ ID NO:6), and GLUT5 (SEQ ID NO:7), shown in [Fig. 3)] Figs. 3A-3D. Skilled artisans will recognize that conserved amino acid residues are more likely to be necessary for preservation of function. Thus, it is preferable that conserved residues are not altered. Alignment of GLUTX with other glucose receptors will reveal regions that are more highly conserved. Such regions are preferably not altered.

Second paragraph on page 80 from about line 23 to page 81 at about line 7:

The human GLUTX gene was identified as follows. A variety of public and proprietary sequence databases were searched using an approach designed to identify putative glucose transporters. This search led to the identification of an EST which was thought likely to encode a portion of a gene having some similarity to genes encoding previously identified glucose transporters. Two PCR primers (TGTTTCCTAGTCTTTGCTACA; SEQ ID NO:8 and TTGTTAAGGCCTTCCATT; SEQ ID NO:9) based on the sequence of the identified EST were used to screen a human mixed tissue cDNA library. This screening resulted in the identification of a probe which was used to screen the human mixed tissue cDNA library. This screening led to the identification of a number of putative glucose transporter clones. A number of these

clones were sequenced and ordered to arrive at a complete sequence for GLUTX. The nucleotide sequence of GLUTX is shown in [Fig. 1] Figs. 1A-1E. The predicted amino acid sequence of GLUTX is also shown in [Fig. 2] Figs. 2A-2D.

Second paragraph on page 82 at about lines 13-27:

The predicted amino acid sequence of GLUTX was compared to the amino acid sequences of GLUT1, (SEQ ID NO:3), GLUT2 (SEQ ID NO:4), GLUT3 (SEQ ID NO:5), GLUT4 (SEQ ID NO:6), and GLUT5 (SEQ ID NO:7). This comparison is depicted in [Fig. 3] Figs. 3A-3D along with a majority sequence (SEQ ID NO:8). As noted above, in designing variant forms of GLUTX which retain the activity of wild-type GLUTX, it is generally preferable to avoid altering residues that are highly conserved. Of course, if one wished to design a reduced activity variant of GLUTX, it is generally preferable to alter conserved residues. Using sequence comparison information one can design GLUTX variants which are more similar to GLUT1, (SEQ ID NO:3), GLUT2 (SEQ ID NO:4), GLUT3 (SEQ ID NO:5), GLUT4 (SEQ ID NO:6), or GLUT5 (SEQ ID NO:7).

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